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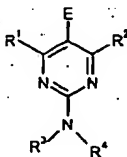
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(54) Title: PROCESS FOR THE PREPARATION OF PYRIMIDINE COMPOUNDS



(I)

(57) Abstract: A process for the preparation of a compound of Formula (I) and intermediates useful therein are provided. The process comprises reacting a compound of formula  $R^1\text{-CO-CH}_2\text{-E}$  with a compound of formula  $R^2\text{-CHX}^1\text{X}^2$  in the presence of a compound of formula  $R^3\text{R}^4\text{N-C(=NH)NH}_2$  and a catalyst, thereby to form a dihydropyrimidine; and oxidising the dihydropyrimidine to form the compound of Formula (I).  $R^1$  is H or an alkyl group;  $R^2$  is H, an alkyl or aryl group;  $R^3$  and  $R^4$  are each independently H, alkyl or aryl, or  $R^3$  and  $R^4$  are linked to form, together with the nitrogen to which they are attached to form a 5 to 7 membered heterocyclic ring; E is H, an unsubstituted alkyl group, an aryl group or an electron withdrawing group; and  $X^1$  and  $X^2$  are each independently leaving groups, or  $X^1$  and  $X^2$  together represent =O.

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/05359

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C07D239/42 C07D239/22

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WATANABE M ET AL: "SYNTHESIS AND BIOLOGICAL ACTIVITY OF METHANESULFONAMIDE PYRIMIDINE-AND N-METHANESULFONYL PYRROLE-SUBSTITUTED 3,5-DIHYDROXY-6-HEPTENOATES, A NOVEL SERIES OF HMG-COA REDUCTASE INHIBITORS" BIOORGANIC & MEDICINAL CHEMISTRY, ELSEVIER SCIENCE LTD, GB, vol. 5, no. 2, 1997, pages 437-444, XP000882043 ISSN: 0968-0896 Scheme 1	1-9, 19-26
A	WO 01/04100 A (LONZA AG ;VEITH ULRICH (CH)) 18 January 2001 (2001-01-18) cited in the application the whole document	1-26
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"Z" document member of the same patent family

Date of the actual completion of the international search

7 April 2004

Date of mailing of the international search report

07. 09. 04

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/05359

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 521 471 A (SHIONOGI & CO) 7 January 1993 (1993-01-07) cited in the application the whole document	1-26
A	BREAUX E J ET AL: "An improved general synthesis of 4-aryl-5-pyrimidinecarboxylates" JOURNAL OF HETEROCYCLIC CHEMISTRY, HETEROCORPORATION. PROVO, US, vol. 18, January 1981 (1981-01), pages 183-184, XP002117468 ISSN: 0022-152X the whole document	1-9, 19-24
X	VANDEN EYNDE, J. J. ET AL: "Microwave-mediated regioselective synthesis of novel pyrimido[1,2- a]pyrimidines under solvent-free conditions" TETRAHEDRON (2001), 57(9), 1785-1791, XP002276336 page 1786, line 1 page 1789; examples 4.3.1-4.3.2	10-13, 15,16
P,X	DE LUCA, LIDIA ET AL: "Cellulose Beads: a New Versatile Solid Support for Microwave-Assisted Synthesis. Preparation of Pyrazole and Isoxazole Libraries" JOURNAL OF COMBINATORIAL CHEMISTRY (2003), 5(4), 465-471, XP002276337 p. 466, col. 2, Scheme 3, compound 3 RN 575838-12-9	25,26

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/05359

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  
1-9, 19-26

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-9,19-26

A process for the preparation of compounds of formulae (1) and (3) and a compound according to claims 25 and 26.  
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2. claims: 10-18

A compound of formula (2a) and a process for its preparation.  
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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/05359

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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